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EXAMINER	
BASHAM, D	
ART UNIT	PAPER NUMBER
1646	3

DATE MAILED: 05/14/98

Please find ~~below~~ attached a communication from the EXAMINER in charge of this application.

Commissioner of Patents

File copy

Office Action Summary	Application No. 08/972,301	Applicant(s) Coleman, et al.
	Examiner Daryl A. Basham	Group Art Unit 1646

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *21-56* is/are pending in the application.

Of the above, claim(s) *39-56* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21, 22, 29, 32, and 36* is/are rejected.

☒ Claim(s) *23-28, 30, 31, 33-35, 37, and 38* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 21-38, drawn to an isolated polypeptide, classified in class 530, subclass 350.

II. Claims 39, 43, 48 and 52, drawn to a compound effective as an agonist of a polypeptide and a method of treatment comprising administration of said agonist, classified in various classes and subclasses as the material composition is not disclosed.

III. Claims 40, 44, 49 and 53, drawn to a compound effective as an antagonist of a polypeptide and a method of treatment comprising administration of said antagonist, classified in various classes and subclasses as the material composition is not disclosed.

IV. Claims 41 and 50 drawn to a method of treatment comprising administration of a polypeptide, classified in class 514, subclass 2.

V. Claims 42 and 51, drawn to gene therapy, classified in class 514, subclass 44.

VI. Claims 45 and 54, drawn to a process for diagnosing a disease by determining a mutation in a nucleic acid encoding a polypeptide, classified in class 435, subclass 6.

VII. Claims 46 and 55, drawn to a process for analyzing for the presence of a polypeptide, classified in class 435, subclass 7.1.

VIII. Claims 47 and 56, drawn to a method for identifying compounds which bind to and activate or inhibit a polypeptide, classified in class 435, subclass 7.2.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I, II and III are independent and distinct, each from the other because they are compositions which possess characteristic differences in structure and function and each have independent utilities, that are distinct for each material composition, which are not interchangeable.

Inventions I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used as an antigen for antibody generation.

Inventions I and Inventions V, VII and VIII are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention I has separate utility such as an antigen for antibody production. See MPEP § 806.05(d).

Inventions I and VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions not disclosed as capable of use together.

Inventions II and Inventions IV-VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions not disclosed as capable of use together.

Inventions III and Inventions IV-VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions not disclosed as capable of use together.

Inventions VI, V, VI, VII and VIII are independent and distinct, each from the other, because the methods are practiced with materially different process steps for materially different purposes.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a

serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

3. During a telephone conversation with Attorney Jay Mullins on April 2, 1998 a provisional election was made with traverse to prosecute the invention of Group I, claims 21-38. Affirmation of this election must be made by applicant in replying to this Office action. Claims 39-56 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 22 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides having substitutions in amino acid sequence such that functional properties are not perturbed, does not reasonably provide enablement for

polypeptides having substitutions where non-functional proteins are generated. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While the specification teaches that polypeptide embodiments can contain substitutions in their amino acid sequences, no relationship between function and specific amino acid residues or function and domain structure is disclosed such that the teachings of the specification are explicit enough to allow for random and non-conservative substitutions to be made. As there is no functional/domain limitation such that variant polypeptides maintain requisite functional fidelity (e.g., cognate ligand binding), the claims embrace molecules which are neither structurally or functionally related to the instant EMAP III. Since it is well known in the art that specific amino acids are essential for proper protein folding, the random substitution of amino acid residues cannot be made indiscriminately given the potential negative effects caused by perturbations in amino acid sequence. In the instant application, non-conservative changes in amino acid sequences are not adequately described by the specification and could not be made using the guidance of the specification because the specification provides no guidance for how to make the appropriate changes in nucleic acid sequence commensurate with the breadth of the claims. In the absence of such information, a person of ordinary skill in the art would be unable to make a functional polypeptide which has 95% identity with amino acids 1-168 of SEQ ID NO: 2 without undue experimentation because selection of mutable sites based on the specification would be arbitrary.

5b. Claims 21 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide encoded by a polynucleotide which is degenerate relative to a naturally occurring polynucleotide, does not reasonably provide enablement for a polypeptide encoded by a polynucleotide which has 95% identity with all possible polynucleotides which are degenerate relative to a naturally occurring polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

By claiming polypeptides using degenerate polynucleotide sequence limitations, all degenerate polynucleotides capable of encoding the amino acid sequence are embraced. If , for example, all of the third positions of the codons are replaceable by wobble hypothesis rules (given nucleic acids of equal length) to give the same amino acid sequence by degeneracy of the genetic code, a nucleic acid having approximately 66.6% identity to the naturally occurring sequence would be expected to be present in the population of molecules. However, a polynucleotide which is 95% identical to said perfectly degenerate polynucleotide (i.e., having 66.6% identity) would not encode the same polypeptide (e.g., frame shifts and termination site changes would produce proteins of undefined function). As such, the limitations of the claims embrace polynucleotides which encode polypeptides that are not envisaged by the specification. Therefore, as the specifications fails to adequately provide guidance or examples of such polypeptides, one skilled

in the art could not make or use the embraced molecules without undue experimentation because such proteins would not have a predictable (assayable) function.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6a. Claims 21, 22, 29, 32 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21, 22, 29, 32 and 36 recite "...% identical". This phrase has unambiguous meaning when it is applied to the comparison of two sequences of equal length, however, sequences of unequal length are evidently considered to be comparable by this standard. It is not clear as to how gaps are to be assessed in determining identity where gaps are required to optimally align two sequences of unequal length. This ambiguity may be demonstrated by the following examples: consider two sequences, ABCDEF and ABEF. These could be compared in four ways:

ABCDEF	4/6 = 67%	ABCDEF	2/6 = 33%
AB---- EF	4/4 = 100%	ABEF	2/4 = 50%

In the absence of a disclosure of the algorithm by which "...% identical" is to be determined, the claims can only be considered definite if comparisons are limited to sequences of identical length. To illustrate this issue, the Examiner has cited George, et al. (1988) which teaches that "the results of the analysis are entirely dependent on the choice of scoring rules"

(page 130, column 2, lines 4-6). It is apparent that an algorithm is required to determine the "% identical".

7. Claims 23-28, 30, 31, 33-35, 37 and 38 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. SEQ ID NOS: 1 and 2 are free of the prior art.

8. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure and shows state of the art in its field but is not determined by the examiner to read upon the invention currently being prosecuted in this application.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daryl A. Basham, Ph.D., whose telephone number is (703) 305-2150. The examiner can normally be reached Monday through Friday from 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

dab
May 11, 1998

Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800